

REMARKS

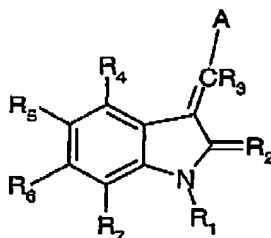
Claims 1 to 15 are pending in the present application. Claims 6-15 are withdrawn from consideration. Claim 1 is rejected under U.S.C. § 112 second paragraph. Claims 1-4, are rejected under 35 U.S.C. 103(a). Additionally, an objection was raised in claim 1 for the manner in which the variable "n" was defined. Applicants have amended claim 1. No new matter has been inserted through this amendment. The rejections are respectfully traversed below.

Rejection of Claim 1 under 35 U.S.C. § 112 second paragraph

The Examiner rejected claim 1 as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. The Examiner objects to the term "isomeric". Applicants have amended claim 1 by changing the term "isomeric" to "stereoisomeric", as suggested by the Examiner. By way of said amendment Applicants respectfully maintain that claim 1 now fully satisfies the requirements of 35 U.S.C. § 112 second paragraph. The withdrawal of this rejection under 35 U.S.C. § 112 second paragraph is requested.

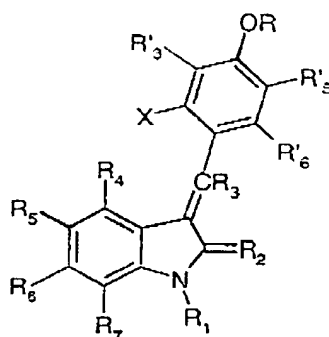
Rejection of Claims 1-4 under 35 U.S.C. § 103 (a)

Claims 1-4, are rejected under 35 U.S.C. § 103(a) as being obvious and thus unpatentable over Tang et al., U.S. Patent 5,886,020, because Tang et al. teach an indoline of formula 1 wherein R₄ and R₅ are H, R₆ is NHC(O)R, R₇ is H, A is a heteroaryl, optionally substituted at one or more positions with an aryl. The Examiner notes that this invention does not disclose a halogen substituent at the aryl ring attached to the heteroaryl group.



formula 1

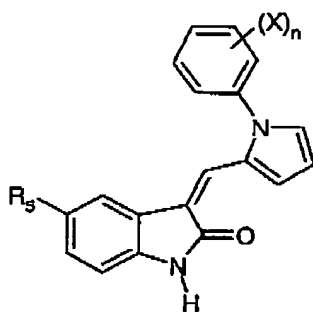
Tang et al. also discloses a compound of formula III, wherein R is H, R₂ is O, R₄ and R₅ are H, R₆ is NHC(O)R, R₇ is H and X is halogen selected from Br, Cl, F or I.



formula III

The Examiner thus maintained that since Tang et al. gives guidance to prepare a compound of formula I and compound of formula III wherein R6 is an amide and R2 is C1-C3? (it is assumed the Examiner meant R2 is O) and X is Cl, Br or F, and thus one of ordinary skill in the art would be motivated to use the teachings of Tang et al. to prepare the instant compounds wherein the phenyl ring is optionally substituted with a halogen because the same reference teaches both compound III and I. Thus, according to the Examiner a *prima facie* case of obviousness has been established.

The Applicants' invention represents a variation of a subgenus as shown in formula II below.



II

wherein R5 is -NH-CO-R2 and -CO-NH-R2 and X is Cl, Br or F.

Accordingly, the guidelines for Examination of said subgenus can be found in the MPEP § 2144.08. MPEP § 2144.08, II states: "The fact that a claimed species or subgenus is encompassed by the prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). Furthermore, at MPEP § 2144.08, I, it is stated: "When evaluating the scope of a claim, every limitation in the claim must be considered. See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). However, the claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole. See, e.g., W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984); Jones

v. Hardy, 727 F.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1983) ("treating the advantage as the invention disregards the statutory requirement that the invention be viewed 'as a whole'").

It is submitted that the Applicants invention was not considered as a whole. In formulating arguments to support the obviousness rejection, it appeared that Applicants' invention was fragmented into structural pieces. Thus, individual structural elements of the claimed invention were highlighted for comparison with the prior art. For example, it appeared that the compound of formula II was broken into structural pieces, that is of an indoline that had an amide substituent, which also had a heteroaryl substituent that in turn had an aryl substituent that in turn had a chloro substituent. Thus dissected, the differences between Tang et al. and the instant invention were noted in order to support an obviousness rejection. It is incorrect to focus on the differences between the prior art and the claimed invention, and then to state the differences themselves or individually are obvious. The claimed invention as a whole is to be considered. See *Lear Siegler, Inc. v. Aeroquip Corp.*, 733 F. 2d 881, 221 USPQ 1025, 1033 (Fed. Cir. 1984). Accordingly, the focus needs to be on the subgenus represented by formula II taken as a whole in comparison to the disclosures found in Tang et al.

Secondly, the single reference cited must provide some motivation to the skilled person to make the invention, for as stated in MPEP § 2144.08, II, 4: "The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound". And furthermore, at 4(a): "Some motivation to select the claimed species or subgenus must be taught by the prior art. See e.g. *Deuel*, 51 F.3d at 1558-59, 34 USPQ2d at 1215".

Tang et al. does not provide motivation to modify the compounds disclosed therein to arrive at the Applicants' invention. Although, Tang et al. has broad generic disclosures of indolines there is no clear teachings found therein that would motivate the skilled artisan to arrive at the claimed subgenus of the instant invention. The Examiner argues that since Tang et al. teaches the potential of adding a halogen to a phenyl ring, which is substituted directly on an indoline ring at the 3-position by a methylene linker, it renders the phenyl ring with halogen substituent of the Applicants' invention obvious. However, as is noted above said phenyl ring of Tang et al. is directly attached through a methylene group to the indoline at the 3-position, which is in contrast to the position of the phenyl group in the Applicants' invention wherein the phenyl group is not attached to the indoline ring, but is substituted upon the 1-position of a pyrrole ring. Compare formula III to formula II. It also must be noted that the disclosure in Tang et al. restricts the halogen (substituent X) to a single position of the phenyl ring and that phenyl ring must also contain the substituent OR meta to said X substituent. In contrast, Applicants' invention does not restrict the halogen substituent to any single position on the phenyl ring and allows for multiple halogens, and does not require a substituent OR on the phenyl ring. To summarize, Tang et al. teaches the desirability of a halogen substituent

coupled with a substituent OR specifically *meta* to said halogen on a phenyl group, with said phenyl group attached to an indoline by a methylene linker, and thus provides no motivation to prepare the compounds of the instant invention, wherein the phenyl group has a different substituent pattern and is not linked to the indoline ring, but is remote to the indoline ring, being substituted at the 1-position (N) of the pyrrole ring.

Furthermore, there is no teaching in Tang et al. to motivate the skilled person to restrict a substituent on the indoline ring to a single position (R5) with the two variables -NH-CO-R2 and -CO-NH-R2 as found in the Applicants' invention. Thus, Tang et al. is silent on the desirability of restricting a substituent at any of positions 4-7 of the indoline ring, and furthermore does not teach the desirability of restricting said substituents (R4, R5, R6 and R7) to -NH-CO-R2 and -CO-NH-R2.

For all the reasons stated above, it is respectfully suggested that a *prima facie* case of obviousness has not been established, and that the rejection of claims 1-4 under 35 U.S.C. § 103 (a) be withdrawn.


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Conclusion

Applicants respectfully submit that claims 1 to 4 are in condition for allowance. Action to that end is requested. In the event the Examiner wishes to contact the undersigned regarding any matter, please call (collect if necessary) the telephone number listed below.

Applicant believes that there are no fees due for this Rule 111 Amendment. However, if the Commissioner deems that fees are due, please charge these fees to Deposit Account No. **18-1982** for Aventis Pharmaceuticals Inc., Bridgewater, NJ. Please credit any overpayment to Deposit Account No. **18-1982**.

Respectfully submitted,



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